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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,722	06/27/2001	Alastair David Griffiths Lawson	1300-1-007	4141

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/674,722	LAWSON ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 10/2/06 is acknowledged and has been entered.

Claims 34-38 are presently being examined.

Applicant's amendment filed 10/2/06 has necessitated the following new ground of rejection.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 34-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed nucleic acid sequence encoding a chimeric receptor, wherein the chimeric receptor contains two independent polypeptide chains recited in instant base claim 34, wherein the spacer domain, the transmembrane domain, and the intracellular domains "comprise" the recited residues from human CD8, CD4 or TCRζ.

The instant claims encompass a nucleic acid molecule that encodes a chimeric receptor wherein the two polypeptide chains are part of a single chain construct, and wherein the spacer domain "comprises" residues 95-159 of human CD8 in which cysteine 143 has been changed to alanine and threonine 117, 118 and 119 have been changed to glycine, alanine, and glycine, respectively, and the transmembrane domains "comprise residues 375 to 395 of CD4, and the intracellular domain of the first polypeptide chain "comprises" residues 396 to 435 of CD4 and the intracellular domain of the second polypeptide chain "comprises" residues 31-142 of TCRζ chain *i.e,* the transmembrane domains may contain the recited portion of any CD4 transmembrane domain with other undisclosed flanking sequences, the spacer domains may contain the recited portion of a modified human CD8 with other undisclosed flanking sequences, and the intracellular signaling domain may contain the recited residues of any CD4 or the human TCRζ chain with other undisclosed flanking sequences unrelated to a human CD4 intracellular

signaling domain or a human TCRζ chain signaling domain, and wherein the chimeric receptor is unable to incorporate into a host cell and signal, or wherein the spacer and/*or* transmembrane domains of the first and second polypeptide chains are selected to remain unassociated, but the two said polypeptide chains do not remain unassociated and signal constitutively.

The specification discloses that plasmids containing nucleic acid molecules, *i.e,* two nucleic acid molecules each encoding one polypeptide chain that make up the chimeric receptor may be transfected into Jurkat cells and the resulting transfected Jurkat cells produce IL-2 in the presence of CD33 positive HL60 target cells *in vitro* (especially page 14 at lines 32-36, abstract and pages 15-16). The specification further discloses that for *ex vivo* use, the DNA may be introduced into effector cells removed from the target host, such cells being CTL, TIL, NK, neutrophils, basophils, TH cells, dendritic cells, B cells haematopoietic stem cells, macrophages, or monocytes, *i.e.,* hematopoietic lineage cells (page 9 at lines 6-21). The specification discloses that a spacer may be any oligo or polypeptide serving to link the association and transmembrain domains of each chain, they may be derived from all or part of naturally occurring molecules such as from all or part of the extracellular region of CD8, CD4 or CD28 or an antibody constant region, including the hinge region, or natural spacing components between functional parts of intracellular signaling molecules, such as spacers between ITAMS, or may be a non-naturally occurring sequence. The specification discloses that the transmembrane domains are chosen or modified to minimize its constitutive association with any other domain in the chimeric receptor but to allow association of the receptor polypeptide chains when ligand is bound by one or more extracellular domains, but does not specify the structure/function relationship for non-association in the absence of ligand, except that the ability of each receptor polypeptide chain to remain unassociated except in the presence of bound ligand may be *enhanced* by incorporating a spacer region between each extracellular association domain and transmembrane domain (page 6 at lines 28-36 and page 7 at lines 1-15). The specification discloses that the spacer domain may be derived from all or part of naturally occurring molecules or may be a non-naturally occurring sequence (paragraph spanning pages 6-7). The specification discloses that transmembrane domains may be any oligo- or poly-peptide and may be derived from a wide variety of sources such as all or part of the alpha, beta or zeta chains of the TCR, CD28, CD8, CD4, CD3 epsilon, CD45 and members of the tetraspan family (paragraph spanning pages 5-6). The specification discloses a chimeric receptor consisting of the components of an anti-CD33 VH and VL, and wherein the spacer, transmembrane and intracellular domains "consist of" rather than "comprise" the elements recited in the instant base claim 34 (page14-15).

One of skill in the art would not have recognized that Applicant was in possession of the necessary common attributes or features possessed by the members of the genus.

Applicant's arguments, of record in the amendment filed 10/2/06 on page 4, have been fully considered but are not persuasive.

It is the Examiner's position that the claim amendments directed to a nucleic acid sequence encoding chimeric receptor is not directed to a receptor comprising specific domains and particular sequences because the recited spacer, transmembrane and intracellular domains "comprise" rather than consist of the recited amino acid sequences, and thus, they may comprise undisclosed flanking amino acid residues of unspecified composition and length. In addition, it is noted by the Examiner that although instant base claim 34 recites "wherein the extracellular ligand association domains of each chain are able to act cooperatively to form a ligand binding site," acting cooperatively to form a ligand binding site is not indicative of a functional downstream signaling event. The chimeric receptor disclosed in the instant specification "consists of" rather than "comprises" the recited elements in the instant claim 34, and when expressed in Jurkat cells, produces a biologically relevant signaling response when challenged with antigen bearing target cells. It is further noted by the Examiner that the recitation of "acting cooperatively to form a ligand binding site" is not a recitation that binding a ligand will result in downstream signaling for a biologically relevant response.

4. No claim is allowed.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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